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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Maha A Hamdan
Medlen & Carroll
Suite 350
101 Howard Street
San Francisco, CA 94105

EXAMINER	
MACAULEY, SHERIDAN R	
ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,480	FREEZE ET AL.	
	Examiner	Art Unit	
	SHERIDAN R. MACAULEY	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *123-166* is/are pending in the application.

4a) Of the above claim(s) *144-152,154,155,157-159 and 162-164* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *123-143,153,156,160,161,165 and 166* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 June 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/14/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A response and amendment were received and entered on August 21, 2008. All evidence and arguments have been fully considered. New claims 151-166 have been added. Claims 123-166 are pending.

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 123-143, in the reply filed on June 15, 2007 was acknowledged in the office action mailed on September 28, 2007. This restriction requirement was deemed proper and was therefore made FINAL.

2. Applicant's reply to the supplemental requirement for restriction mailed on June 5, 2008 was received on August 28, 2008. Applicant's election with traverse of "heparan sulfate" as the species of group A and the step (d) recited in claim 160 as the species of group B, as set forth in the restriction requirement mailed on June 5, 2008, is acknowledged. The traversal is on the ground(s) that lack of unity of invention has not been established. This is not found persuasive because the species do not relate to a single general inventive concept under PCT rule 13.1 because, under PCT rule 13.2, the species lack the same or corresponding special technical features for the following reasons. The technical feature that is common to all claims is the BAP-oligosaccharide taught by Toomre et al. (Glycobiology, 5:653-663; document cited in prior action), as set forth in the previous restriction requirement. Further, the technical feature that is common to the species is the method recited in claim 135, which is rendered obvious by Varkas, Schmidt and Hodges, as set forth in the office action mailed on September 28,

2007 and discussed below. Therefore, there is no special technical feature that is common to all species. Applicant's argument that the previous requirement for restriction was confusing in that it referred to incorrect claim numbers is also noted. However, although the argument may have been unclear insofar as the claim numbers referred to therein were incorrect, it is noted that the arguments are still deemed valid in that they set forth the lack of unity of invention rephrased above and discussed in the actions mailed on September 28, 2007 and June 5, 2008. Applicant further argues that the restriction requirement is improper because it relates in dependent claims rather than independent claims. It is noted, however, that a claim may also contain a reference to another claim even if it is not a dependent claim (MPEP 1850). The method recited in claim 135 relates to claim 123 insofar as it refers to a method of using the product procured by the method of the claim from which it depends. In this situation, it is deemed that claim 135 is not a dependent claim. Furthermore, although applicant argues that restriction between the species is improper because it relates to dependent claims 151-155, 136 and 157-162, it is noted that, since the genus does not make a contribution over the prior art and the species are directed to alternatives of a dissimilar nature, the election of species is proper (see MPEP 1850). The requirement is still deemed proper and is therefore made FINAL.

3. Claims 144-150, 151-152, 154-155, 157-159 and 162-164 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected groups and species, there being no allowable generic or linking claim. Although applicant states in the reply that claims 151 and 154-155 read on the elected species (see p. 11, section

3), it is noted that these claims have been withdrawn because they recite alternatives in the genus, as set forth in the requirement for restriction, and because they do not recite the elected species "heparan sulfate."

4. Claims 123-143, 153, 156, 160-161 and 165-166 are examined on the merits in this office action.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 156 and 161 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 156 and 161 are rendered indefinite by the recitation of "amino acids 1 to 12 of annexin I." It is unclear whether applicant intends for the claim to be interpreted that the glycan binds to any of amino acids 1 to 12 on annexin I, the portion of annexin I from amino acid position 1 to amino acid position 12, or some other alternative. Therefore, the metes and bounds of the claim would be unclear to one of ordinary skill in the art.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 142 and 143 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

10. It is apparent that the claimed antibodies (mAbEE4.1, mAbGB3.1, mAbB2.6, and mAbEH2.7) are required to practice the claimed invention. As such the biological material must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not obtainable or available, the requirement of 35 USC 112, first paragraph may be satisfied by a deposit of the biological material.

11. The process disclosed in the specification does not appear to be repeatable, it is not clear that the invention will work with commonly available material and it is not apparent if the biological materials are both known and readily available to the public.

12. If a deposit has been made under the terms of the Budapest Treaty, then a statement, affidavit or declaration by applicant, or a statement by an attorney of record over his or her signature and registration number, or someone empowered to make such a statement, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

13. If a deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-

2411.05, applicant may provide assurance of compliance by statement, affidavit or declaration, or by someone empowered to make the same, or by a statement by an attorney of record over his or her signature and registration number showing that:

a. during the pendency of the application, access to the invention will be afforded to the Commissioner upon request;
b. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
c. the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last requires or for the enforceable life of the patent, whichever is longer;
d. a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and
e. the deposit will be replaced if it should ever become inviable.

14. Regarding applicant's argument that the recited antibodies are readily obtainable by a repeatable method set forth in the specification, it is noted that, although the specification sets forth a method for making antibodies that possess characteristics similar to those recited above, all characteristics of the claimed antibodies are not described in such a way as to allow one of ordinary skill in the art a method of exactly reproducing the antibodies recited in the claims. Therefore, the antibodies recited in the claims must be made readily available to the public.

15. A Statement of Biological Deposit was filed in this application on January 28, 2008. Applicant states that a biological deposit will be made in this application during pendency of the application (i.e., on or before payment of the issue fee). This is respectfully noted and applicant may choose to delay to deposit the biological material until a time when all other claims in the application are in condition for allowance. However, since no biological deposit has yet been made, the rejection of those claims reciting the biological material stands until such a time.

16. Claims 136 and 160-161 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying a test agent which reduces binding to specific carboxylated glycans, does not reasonably provide enablement for identifying the test agent as reducing inflammation in a tissue comprising endothelial cells expressing said carboxylated glycan. Claim 136 recites the method of claim 135 (as described below) further comprising (d) identifying said test agent as reducing inflammation or cancer. Claims 160 and 161 recite the method of claim 135 further comprising (d) identifying said test agent as reducing growth of cancer cells that express said carboxylated glycan, specifically wherein said carboxylated glycan that is expressed by said cancer cells binds to a molecule comprising one or more of S100A8, S100A9, S10012, amphoterin, annexin I and amino acids 1 to 12 of annexin I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

17. In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or

unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. In the instant case, those factors deemed most relevant are the quantity of experimentation necessary, the state of the prior art, the predictability or unpredictability of the art and the breadth of the claims.

18. The disclosure is not enabling for identifying a test agent as reducing inflammation or cancer because it does not present enough direction and guidance for one skilled in the art to use the invention with a reasonable expectation of success without undue experimentation. Although the disclosure provides guidance for the identification of an agent which reduces inflammation related to the binding of the proteins annexin I, S100A8/A9 and amphoterin, the disclosure does not provide any guidance or working examples to direct one to the development of a screening method that would identify any test agent that reduces inflammation or cancer. In particular, there are no working examples presented that would enable one of ordinary skill in the art to identify any test agent that reduces cancer. The state of the prior art indicates that the identification of an agent that reduces cancer in vitro does not adequately predict the effect of the drug when used to treat a cancer patient in vivo (see Zips et al., 2005, In vivo, 19:1-7, p. 3, col. 2, par. 3). One would thus be required to screen a test agent in vivo to identify such an agent as reducing cancer, requiring undue experimentation for one of ordinary skill in the art to use the invention as claimed. Further, applicant discloses in the specification that a cascade of molecular events is involved in the production of an inflammatory response, particularly in the recruitment of

leukocytes (see specification, pp. 1-3). There is no guidance provided to detect agents that reduce inflammation by pathways other than those disclosed. Due to the complexity of molecular events involved in the production of an inflammatory response, one would be unable to predict whether a test agent would reduce inflammation without undue experimentation. Given these facts, one skilled in the art would be unable to predict whether the claimed method for the identification of agents that reduce inflammation or cancer could be performed with a reasonable expectation of success.

19. Therefore, the disclosure of the instant application does not enable one skilled in the art to use the invention as claimed.

Claim Rejections - 35 USC § 102

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

21. Claims 123-128, 130, 131, 133, 134, 165 and 166 are rejected under 35 U.S.C. 102(b) as being anticipated by Varki et al. (US 5,449,781). Claim 123 recites a method for purifying a carboxylated glycan, said method comprising: (a) providing: (i) a molecule comprising a carboxylated glycan; (ii) biotinylated diamino pyridine (BAP); and (iii) an exoglycosidase; (b) conjugating said molecule to said BAP to produce a BAP-glycan conjugate; (c) treating said BAP-glycan conjugate with said exoglycosidase to produce a first treated BAP-glycan conjugate comprising a first anionic BAP-glycan

conjugate having from 1 to 2 negative charges per molecule; and (d) isolating said first anionic BAP-glycan conjugate having 1 to 2 negative charges per molecule, thereby purifying a carboxylated glycan. Claim 124 recites the method of claim 123, further comprising the steps of: (e) treating said first anionic BAP-glycan conjugate produced in step (e) or (d) with an exoglycosidase to produce a second anionic treated BAP-glycan conjugate comprising a second anionic BAP-glycan conjugate having from 1 to 2 negative charges per molecule; and (f) isolating said second anionic BAP-glycan conjugate having 1-2 negative charges per molecule, thereby purifying a carboxylated glycan. Claim 125 recites the method of 124, further comprising repeating steps (e) and (f) from 1 to 10 times. Claim 126 recites the method of claim 123 wherein said isolating comprises fractionating by ion exchange chromatography. Claim 127 recites a carboxylated glycan purified by the method of claim 123. Claim 128 recites the glycan of claim 127, wherein the molecule is a glycoprotein or polysaccharide, specifically a receptor for advanced glycation end products (RAGE). Claim 130 recites a method for purifying a carboxylated glycan, said method comprising: (a) providing a molecule comprising a carboxylated glycan; (b) isolating from said molecule a first anionic glycan containing from 1 to 4 negative charges per molecule; and (c) desialylating said isolated first anionic glycan to produce a first desialylated anionic glycan containing from 1 to 4 negative charges per molecule, thereby purifying a carboxylated glycan. Claim 131 recites the method of claim 130, further comprising (d) isolating from said first disialylated anionic glycan per molecule, thereby purifying a carboxylated glycan. Claims 133 and 134 recite a carboxylated glycan purified by the method of claim 130,

specifically wherein the molecule is a glycoprotein or a polysaccharide. Claims 165 and 166 recite the method of claim 130 wherein the first desialylated anionic glycan in steps (c) and (d) have from 1 to 3 negative charges per molecule.

22. Varki teaches a method for purifying a carboxylated glycan (e.g. those containing siacylic acid residues) comprising conjugating a carboxylated glycan with BAP; treating the BAP-glycan conjugate with an exoglycosidase (sialidase); and isolating the BAP-glycan conjugate (by HPLC), thereby purifying the glycan (col. 9, line 51-col. 10, line 8, col. 10, lines 47-62). Although Varki does not specifically teach that the BAP-glycan conjugate has 1-2 negative charges per molecule, the process uses a number of conjugates that would inherently have the claimed charges. Varki teaches that the BAP-glycan conjugate produced by the claimed process may be further treated with exoglycosidases to produce further BAP-glycan conjugates, which may further be purified, and that this process may be repeated one or more times (col. 11, lines 7-26). Varki teaches that isolating the BAP-glycan conjugate may comprise ion exchange chromatography (col. 11, lines 53-57). The method of Varki comprises the steps of providing a molecule comprising a carboxylated glycan (the BAP-glycan conjugate); isolating from the molecule a first anionic glycan containing from 1-4 charges; desialylating the isolated first anionic glycan to produce a desialylated anionic glycan containing from 1-4 negative charges; and isolating from the first glycan a second anionic glycan containing from 1-4 negative charges (col. 9, line 51-col. 10, line 8, col. 10, lines 47-62; col. 11, lines 53-57). Varki teaches a purified carboxylated glycan, and

that the molecule which comprises the glycan can be a polysaccharide (col. 9, line 66-col. 10, line 8).

23. Therefore, Varki anticipates all of the limitations of the cited claims.

Claim Rejections - 35 USC § 103

24. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

25. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

26. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

27. Claims 123-128, 130-135, 137, 138, 140, 141, 153, 156, 165 and 166 are rejected under 35 U.S.C. 103(a) as being unpatentable over Varki et al. (US 5,449,781) in view of Schmidt et al. (Biochimica et Biophysica Acta, 2000, 99-111) and Hodges et al. (US 5,738,996). Claim 123 recites a method for purifying a carboxylated glycan, said method comprising: (a) providing: (i) a molecule comprising a carboxylated glycan; (ii) biotinylated diamino pyridine (BAP); and (iii) an exoglycosidase; (b) conjugating said molecule to said BAP to produce a BAP-glycan conjugate; (c) treating said BAP-glycan conjugate with said exoglycosidase to produce a first treated BAP-glycan conjugate comprising a first anionic BAP-glycan conjugate having from 1 to 2 negative charges per molecule; and (d) isolating said first anionic BAP-glycan conjugate having from 1-2 negative charges per molecule, thereby purifying a carboxylated glycan. Claim 124 recites the method of claim 123, further comprising the steps of: (e) treating said first anionic BAP-glycan conjugate produced in step (e) or (d) with an exoglycosidase to produce a second anionic treated BAP-glycan conjugate comprising a second anionic BAP-glycan conjugate having from 1 to 2 negative charges per molecule; and (f) isolating said second anionic BAP-glycan conjugate having from 1-2 negative charges per molecule, thereby purifying a carboxylated glycan. Claim 125 recites the method of 124, further comprising repeating steps (e) and (f) from 1 to 10 times. Claim 126 recites the method of claim 123 wherein said isolating comprises fractionating by ion exchange chromatography. Claim 127 recites a carboxylated glycan purified by the method of

claim 123. Claim 128 recites the glycan of claim 127, wherein the molecule is a glycoprotein or polysaccharide. Claim 130 recites a method for purifying a carboxylated glycan, said method comprising: (a) providing a molecule comprising a carboxylated glycan; (b) isolating from said molecule a first anionic glycan containing from 1 to 4 negative charges per molecule; and (c) desialylating said isolated first anionic glycan to produce a first desialylated anionic glycan containing from 1 to 4 negative charges per molecule, thereby purifying a carboxylated glycan. Claim 131 recites the method of claim 130, further comprising (d) isolating from said first disialylated anionic glycan, thereby purifying a carboxylated glycan. Claim 132 recites the method of claim 130, further comprising a step of treating the molecule with a proteinase enzyme prior to step (a). Claims 133 and 134 recite a carboxylated glycan purified by the method of claim 130, specifically wherein the molecule is a glycoprotein or a polysaccharide. Claim 135 recites a method for identifying a test agent as reducing specific binding of a polypeptide to a carboxylated glycan, comprising: (a) providing: (i) a carboxylated glycan purified by the method of claim 1; (ii) an antibody that specifically binds to said carboxylated glycan, wherein said binding is not reduced by a carboxylate-neutralized glycan; and (iii) a test agent; (b) contacting said purified carboxylated glycan, said antibody, and said test agent; and (c) detecting a reduction in the level of binding of said antibody to said carboxylated glycan in the presence of said test agent compared to in the absence of said test agent, thereby identifying said test agent as reducing specific binding of a polypeptide to a carboxylated glycan. Claim 137 recites the method of claim 135, wherein the glycan is attached to a solid surface. Claim 138 recites the

method of claim 135 wherein the molecule is a glycoprotein or polysaccharide. Claims 140 and 141 recite the method of claim 135, wherein the antibody is monoclonal, specifically an IgG antibody. Claim 153 recites the method of claim 135 wherein said antibody does not specifically bind to heparan sulfate. Claim 156 recites the method of claim 136 wherein said carboxylated glycan that is expressed by said endothelial cells binds to a molecule comprising one or more of S100A8, S100A9, S10012, amphoterin, annexin I and amino acids 1-12 of annexin I. Claims 165 and 166 recite the method of claim 130 wherein the first desialylated anionic glycan in steps (c) and (d) have from 1 to 3 negative charges per molecule.

28. Varki teaches a method for purifying a carboxylated glycan (e.g. those containing siacylic acid residues) comprising conjugating a carboxylated glycan with BAP; treating the BAP-glycan conjugate with an exoglycosidase (sialidase); and isolating the BAP-glycan conjugate (by HPLC), thereby purifying the glycan (col. 9, line 51-col. 10, line 8, col. 10, lines 47-62). Although Varki does not specifically teach that the BAP-glycan conjugate has 1-2 negative charges per molecule, the process may use a number of conjugates that would inherently have the claimed charges. Varki teaches that the BAP-glycan conjugate produced by the claimed process may be further treated with exoglycosidases to produce further BAP-glycan conjugates, which may further be purified, and that this process may be repeated one or more times (col. 11, lines 7-26). Varki teaches that isolating the BAP-glycan conjugate may comprise ion exchange chromatography (col. 11, lines 53-57). The method of Varki comprises the steps of providing a molecule comprising a carboxylated glycan (the BAP-glycan conjugate);

isolating form the molecule a first anionic glycan containing from 1-4 charges; desialylating the isolated first anionic glycan to produce a desialylated anionic glycan containing from 1-4 negative charges; and isolating from the first glycan a second anionic glycan containing from 1-4 negative charges (col. 9, line 51-col. 10, line 8, col. 10, lines 47-62; col. 11, lines 53-57). Varki teaches a purified carboxylated glycan, and that the molecule which comprises the glycan can be a polysaccharide (col. 9, line 66-col. 10, line 8). Varki teaches a method for screening recombinant protein libraries using the BAP-conjugated glycans to identify proteins that bind to the saccharides (col. 7, lines 17-25). Varki teaches that IgG antibodies can be produced which specifically bind to the purified glycans (col. 7. lines 8-13).

29. Varki does not teach a step of treating the molecule with a proteinase prior to step (a) of the process recited in claim 130. Varki does not specifically teach a method for identifying a test agent that reduces specific binding of a polypeptide to a carboxylated glycan.

30. Hodges teaches a test method wherein a labeled antigen, which may be immobilized, is bound to an antibody and a test agent, wherein the reduction of the level of binding of the antibody to the antigen is detected and is indicative of specific binding of the test agent to the antigen (col. 13, lines 28-44, col. 14, lines 6-15).

31. At the time of the invention, a method for purifying a carboxylated glycan comprising nearly all of the claimed elements was known, as taught by Varki. It was further known at the time of the invention that tests could be conducted to detect the specific binding of a test agent by measuring the reduction in the specific binding of an

antibody, as taught by Hodges. The treatment of a composition comprising an oligosaccharide with a protease prior to purification would have been a matter of routine experimentation for one of ordinary skill in the art in order to remove any proteins that may be bound to the oligosaccharides. One or ordinary skill in the art would have been motivated to combine these teachings because Varki teaches that it would be desirable to use the methods to screen for proteins which bind to the saccharides, and that the methods enable the production of antibodies specific for the saccharides (col. 7, lines 18-21). Hodges teaches a method using antibodies to screen for proteins that bind to an antigen. One would therefore have recognized that it would be desirable to use the methods of Hodges in combination with the method taught by Varki. Furthermore, it would have been considered a matter of obviousness to produce antibodies with desirable characteristics, such as those which bind to saccharides of interest but do not bind to cellular components such as heparan sulfate, or to test endothelial cells comprising a carboxylated glycan. One of ordinary skill in the art would have had a reasonable expectation of success in combining these teachings because Varki teaches all of the required elements, and Hodges teaches simplified screening methods. It would therefore have been obvious to one of ordinary skill in the art to combine the teachings discussed above to arrive at the claimed invention.

32. Claims 123-135, 137-141, 153, 156, 165 and 166 are rejected under 35 U.S.C. 103(a) as being unpatentable over Varki et al. (US 5,449,781) in view of Hodges et al. (US 5,738,996), as applied to claims 123-128, 130-135, 137, 138, 140, 141, 153,

156, 165 and 166 above, and further in view of Schmidt et al. (Biochimica et Biophysica Acta, 2000, 99-111). Claims 123-128, 130-135, 137, 138, 140, 141, 153, 156, 165 and 166 have been discussed above. Claims 129 and 139 recite the glycan of claims 127 and 135, wherein the molecule is a glycoprotein or polysaccharide, specifically a receptor for advanced glycation end products (RAGE).

33. Varki teaches a method for purifying a carboxylated glycan (e.g. those containing siacylic acid residues) comprising conjugating a carboxylated glycan with BAP; treating the BAP-glycan conjugate with an exoglycosidase (sialidase); and isolating the BAP-glycan conjugate (by HPLC), thereby purifying the glycan (col. 9, line 51-col. 10, line 8, col. 10, lines 47-62). Although Varki does not specifically teach that the BAP-glycan conjugate has 1-2 negative charges per molecule, the process may use a number of conjugates that would inherently have the claimed charges. Varki teaches that the BAP-glycan conjugate produced by the claimed process may be further treated with exoglycosidases to produce further BAP-glycan conjugates, which may further be purified, and that this process may be repeated one or more times (col. 11, lines 7-26). Varki teaches that isolating the BAP-glycan conjugate may comprise ion exchange chromatography (col. 11, lines 53-57). The method of Varki comprises the steps of providing a molecule comprising a carboxylated glycan (the BAP-glycan conjugate); isolating form the molecule a first anionic glycan containing from 1-4 charges; desialylating the isolated first anionic glycan to produce a desialylated anionic glycan containing from 1-4 negative charges; and isolating from the first glycan a second anionic glycan containing from 1-4 negative charges (col. 9, line 51-col. 10, line 8, col.

10, lines 47-62; col. 11, lines 53-57). Varki teaches a purified carboxylated glycan, and that the molecule which comprises the glycan can be a polysaccharide (col. 9, line 66-col. 10, line 8). Varki teaches a method for screening recombinant protein libraries using the BAP-conjugated glycans to identify proteins that bind to the saccharides (col. 7, lines 17-25). Varki teaches that IgG antibodies can be produced which specifically bind to the purified glycans (col. 7. lines 8-13).

34. Hodges teaches a test method wherein a labeled antigen, which may be immobilized, is bound to an antibody and a test agent, wherein the reduction of the level of binding of the antibody to the antigen is detected and is indicative of specific binding of the test agent to the antigen (col. 13, lines 28-44, col. 14, lines 6-15).

35. It would have been obvious at the time of the invention to combine the teachings of Varki and Hodges to develop the claimed methods, as discussed above. However, neither Varki nor Hodges teaches that the molecule comprising the glycan is a glycoprotein such as RAGE.

36. Schmidt teaches that RAGE is receptor protein for advanced glycation end products (AGEs; abstract, p. 100, col. 2, par. 2).

37. At the time of the invention, methods for purifying a carboxylated glycan and identifying a test agent comprising nearly all of the claimed elements were known, as taught by Varki and Hodges. The RAGE protein was also known at the time of the invention, as taught by Schmidt. One of ordinary skill in the art would have been motivated to combine these teachings because Varki teaches that it would be desirable to produce BAP conjugates with glycoproteins as well as oligosaccharides (col. 1, lines

48-59). One of ordinary skill in the art would have had a reasonable expectation of success in combining these teachings because Varki teaches that the process may be used to purify any molecule with a bound glycan, such as RAGE. Moreover, RAGE was a known protein at the time of the invention. The discovery that a previously known protein has previously unknown elements (e.g. bound glycans) does not render the use of that protein with a known method novel. It would therefore have been obvious to one of ordinary skill in the art to combine the teachings discussed above to arrive at the claimed invention.

38. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Response to Arguments

39. Applicant's arguments filed January 28, 2008 have been fully considered but they are not persuasive. Applicant argues that the disclosure of the instant application is fully enabled so as to allow one of ordinary skill in the art to use the invention as claimed. Applicant argues that Varki does not anticipate or render obvious the claimed invention because the reference does not teach certain features of the claims. Applicant argues that there is no reasonable expectation of success in combining the teachings of Varki, Hodges and Schmidt to arrive at the claimed invention.

40. In response to applicant's argument that the disclosure of the instant application is fully enabled so as to allow one of ordinary skill in the art to use the invention as

claimed, it is noted that, although applicant argues that no undue experimentation would be required for one of ordinary skill in the art to use the invention as claimed to identify a test agent that is capable of reducing cancer, the disclosure does not enable one of ordinary skill in the art to practice the invention in order to find any agent that is capable of reducing cancer. Although examples have been given to provide guidance to one of ordinary skill in the art to identify agents that may reduce inflammation as related to the binding of specific proteins, no working examples have been provided to give one of ordinary skill in the art to practice the claimed method in order to identify agents that may reduce cancer, particularly by pathways other than those disclosed, as discussed above. Therefore, applicant's specification is not fully enabled to provide guidance to one of ordinary skill in the art to practice the invention as claimed.

41. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the isolation of a fraction of BAP-glycan conjugates having 1-2 or 1-4 negative charges per molecule from those that do not have the number of charges per molecule recited in the claims) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). For instance, the claims recite "isolating said first anionic BAP-glycan conjugate having from one 1-2 negative charges per molecule," but do not recite what the conjugate is isolated from, what is excluded in the isolation, or the purity of the resultant conjugate composition. The process of Varki uses a number of conjugates that would inherently

have the claimed charges and teaches a step for the purification of the conjugates. Therefore, the process of Varki teaches isolating conjugates having the charges recited in the claims. Although applicant argues that Varki does not teach the features of claim 130, it is noted that the reference teaches the following: isolating a first anionic glycan containing from 1-4 charges (col. 9, line 51-col. 10, line 8), desialylating the isolated first anionic glycans to produce a desialylated anionic glycans containing from 1-4 negative charges (col. 10, lines 47-62) and isolating from the first glycans a second anionic glycans containing from 1-4 negative charges (col. 11, lines 53-57). Furthermore, Varki specifically teaches the preparation of conjugates having from 1-2 negative charges per molecule (col. 10, lines 1-2). The specification therefore teaches the features recited in the claims and the feature to which applicant's arguments are directed is not recited in the instant claims.

42. Regarding applicant's argument that there is no reasonable expectation of success in combining the teachings of Varki, Hodges and Schmidt to arrive at the claimed invention, it is noted that the method of the claimed invention was known at the time of the invention, as discussed above. Although Varki does not teach the use of the method to purify RAGE, the reference teaches that the process may be used to purify a molecule with a bound glycan. In addition to the rationale set forth in the rejection above, the choice from a finite number of identified, predictable solutions (e.g., the choice of RAGE from a finite number of molecules meeting Varki's criteria), with a reasonable expectation of success may be used to support a finding of obviousness (see MPEP 2143). One of ordinary skill in the art would have had a reasonable

expectation of success in using RAGE in the method rendered obvious by the references cited above because the references teach that a methods comprising all of the elements recited in the claims were known in the art at the time of the invention, and that such methods could have been used with a molecule such as RAGE. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in practicing the method of the combined prior art.

43. Therefore, applicant's arguments have been fully considered, but they have not been found to be persuasive.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHERIDAN R. MACAULEY whose telephone number is (571)270-3056. The examiner can normally be reached on Mon-Thurs, 7:30AM-5:00PM EST, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SRM

/Ruth A. Davis/
Primary Examiner, Art Unit 1651